REMARKS

Amendments to the Claims

Claims 1-25 are currently pending. Claims 1 and 6 have been amended. Claims 12 and 16-19 were previously canceled without prejudice or disclaimer. Claims 4-5, 7, 13-15, and 20-25 were previously withdrawn as drawn to a non-elected invention.

Claim 1 has been amended to recite a method for identifying a candidate beta catenin modulating agent comprising, among other steps, the steps of: (e) providing a second assay system capable of detecting a change in the activity of beta catenin comprising cultured cells expressing PRKC-ι; (f) contacting the assay system of step (e) with the candidate test agent of step (b); (g) measuring the activity of beta catenin in the presence or absence of the test agent; and (h) confirming that the test agent of step (b) is a candidate beta catenin modulating agent by detecting a change in the activity of beta catenin in the presence or absence of the test agent. Support for the amendments can be found throughout the specification and particularly at pages 35-36 and 41-42.

Claim 6 has been amended to recite that the second assay system is selected from a nuclear beta catenin measurement assay and a beta catenin gene reporter assay. Support for the amendment can be found at, for example, page 42.

The claim amendments are made solely in an effort to advance prosecution and are made without prejudice, without intent to acquiesce in any rejection of record, and without intent to abandon any previously claimed subject matter. No new matter has been added by way of these amendments.

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Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Claims 1-3, 6, and 8-11 were rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse the rejections.

The Office alleged that claims 1-3, 6, and 8-11 are indefinite because they recite "the beta catenin pathway", which is, according to the Office, a network of signal transduction pathways, not just a single pathway. The Office concludes that one of skill in the art would not know to which pathway the claims refer.

Without acceding to the merits of the rejection, Applicants submit that the claims have been amended to delete reference to the “beta catenin pathway” and instead recites a method of identifying a candidate beta catenin modulating agent comprising, among others, the steps of detecting a change in the expression of PRKC-ι in the presence of the test agent compared with no test agent in a first assay system and detecting a change in the activity of beta catenin (protein) in the presence or absence of the test agent in a second assay. Applicants submit that one skilled in the art would understand what is meant by the term “beta catenin” and thus the claims as amended are clear and definite.

In addition, the Office stated that claims 1-3, 6, and 8-11 are indefinite because they require the step of "measuring the beta catenin pathway" and it is allegedly not clear how one measures an entire pathway or what is intended by "measuring the beta catenin pathway". Without acceding to the merits of the rejection, Applicants submit that the claims have been amended to delete reference to “measuring the beta catenin pathway” and instead recites “measuring the activity of beta catenin” (protein). Applicants submit that one skilled in the art would understand from the teaching in the specification and the knowledge in the art how to measure the activity of a protein, including beta catenin, and thus the claims as amended are clear and

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definite.

Rejection of Claims Under 35 U.S.C. § 103

Claims 1, 2, 6, 8, and 9 stand rejected under 35 U.S.C. 103 as allegedly being unpatentable in view of Murray et al (J. Biol. Chem., 272:27521-27524 (1997)) ("Murray"). Applicants respectfully traverse the rejections.

According to the Office, Murray examined the role of PKC iota in drug-induced (okadaic acid and taxol) apoptosis in K562 cells and found that K562 cells that overexpress PKC iota had an enhanced resistance to drug-induced apoptosis, whereas cells that under-expressed PKC iota were more susceptible to drug-induced apoptosis.

With respect to the claimed invention, the Office stated that steps (a)-(d) are anticipated by Murray, which teaches a first assay system in which the effect of antisense against PKC iota expression is measured. The Office maintained that the step of "identifying a beta catenin modulating agent" is inherent in the active steps carried out by Murray, i.e. in detecting a change in PKC iota expression.

In addition, the Office maintained that Murray further provided a second assay system in which the effect of antisense PKC iota on drug-induced apoptosis was measured in K562 cells. The Office maintained that it would have been obvious to contact that system with the same PKC iota antisense used in the first system to assess the effect on drug-induced apoptosis, and, in so doing, one would practice steps (f)-(h) of claims 1, 2, 6, 8, and 9. The limitation of "measuring the beta catenin pathway" in step (g) was considered to be met by Murray's assays of apoptosis because, according to the Office, beta catenin was known to be involved in the induction of apoptosis, and therefore all steps downstream of beta catenin in this process, including the DNA fragmentation and nuclear morphological changes assayed by Murray, would be considered as part of "the beta catenin pathway".

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However, to meet the requirements for a *prima facie* case of obviousness, the Office must demonstrate that the references teach or suggest all the limitations of the claims. Post-KSR, the Board of Patent Appeals and Interferences (BPAI) has continued to maintain that:

> [A]n examiner must make "a searching comparison of the claimed invention — *including all its limitations* - with the teaching of the prior art." *In re Ochiai,* 71 F.3d 1565, 1572 (Fed. Cir. 1995) (emphasis added). Thus, "obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.,* 349 F.3d, 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka,* 490 F.2d 981, 985 (CCPA 1974)). *Ex Parte* Wada, BPAI, Appeal 2007-377, page 7 (Jan. 15, 2008) (unpublished). *See also, Ex parte* Shepard, BPAI, Appeal 2008-0401, page 7 (Jan. 3, 2008)(unpublished).

Applicants submit that Murray fails to teach or suggest a method for identifying a candidate beta catenin modulating agent using a double assay system that involves measuring and detecting a difference in the expression of PRKC- iota in the presence and absence of a test agent and measuring and detecting a change in the activity of beta catenin in the presence and absence of a test agent. First, Murray is not concerned at all with beta catenin and thus provides no teaching or suggestion whatsoever relating to beta catenin or the pursuit of agents that modulate beta catenin. Further, given that Murray does not even mention beta catenin, it provides no teaching whatsoever relating to this protein or its function, much less its role in cellular pathways, including apoptosis. Finally, in the absence of any mention whatsoever of beta catenin, Murray in particular fails to teach or suggest a connection between PRKC-iota and beta catenin such that one skilled in the art would recognize that an agent that regulates PRKC-iota expression could be a beta catenin modulating agent. In view of the complete absence of teaching concerning beta catenin and particularly in view of the lack of teaching with respect to its relationship with PRKC-iota, Murray fails to teach or suggest the claimed double assay method of identifying a candidate beta catenin modulating agent. Specifically, Murray fails to teach or

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suggest using a first assay system to detect a change in the expression of PRKC-ι in the presence or absence of a test agent and then using a second assay system to detect a change in the activity of beta catenin in the presence or absence of the test agent.

Moreover, Murray's measurement of drug-induced apoptosis in K562 cells that over- or under-express PRCK-iota does not render obvious a method of identifying a candidate beta catenin modulating agent using, among other things, an assay system that detects a change in the activity of beta catenin in the presence or absence of a test agent. First, Murray's teaching is limited to an indication that PRCK-iota may play a role in drug-induced apoptosis in K562 cells. However, with respect to natural cellular apoptosis, Murray actually teaches that PRCK-iota expression has no effect on apoptosis (as measured by DNA morphology; see Figure 4D). Further, Murray provides no teaching whatsoever as to the proteins that may be regulated by PRCK-iota in either the drug-induced or natural apoptotic pathway.

Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness because Murray fails to teach or suggest all of the limitations of the claimed methods. Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) rejection based on Murray.

Claims 1, 2, 6, 8, and 9 were rejected under 35 U.S.C. 103(a) as being unpatentable over Cowsert et al (US 20040014049) ("Cowsert") and Murray et al (J. Biol. Chem. 272(44): 27521-27524, 1997). Applicants respectfully traverse the rejections.

According to the Office, Cowsert teaches methods of inhibiting the expression of PKC iota in cultured cells by contacting the cells with an antisense oligonucleotide directed against PKC iota mRNA. Thus, the Office concluded that Cowsert teaches steps (a)-(d) of claims 1, 2, 6, and 8-10. Although the Office admitted that Cowsert does not explicitly teach instant method steps (e)-(g), it asserted that Cowsert suggests the further use of the antisense oligonucleotides in studying PKC iota function by analyzing gene expression

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patterns in a variety of settings, including disease association, signaling pathways, and cellular localization. The Office argued that it would have been obvious to one of ordinary skill in the art to have used the antisense oligonucleotides of Cowsert to down-regulate PKC-iota expression in K562 cells to measure drug-induced apoptosis in the presence and absence of the oligonucleotides, which procedure would have met the limitations of instant steps (e)-(g), for the reasons previously discussed with respect to Murray.

As discussed above, to meet the requirements for a *prima facie* case of obviousness, the Office must demonstrate that the combination of references teach or suggest all the limitations of the claims. However, Applicants submit that Cowsert and Murray, alone or in combination, fail to teach or suggest a method for identifying a candidate beta catenin modulating agent using a double assay system that involves measuring and detecting a difference in the expression of PRKC- iota in the presence and absence of a test agent and measuring and detecting a change in the activity of beta catenin in the presence and absence of a test agent. Like Murray, the Cowsert reference is not concerned at all with beta catenin and thus provides no teaching or suggestion whatsoever relating to beta catenin or the pursuit of agents that modulate beta catenin. Further, given that Cowsert does not even mention beta catenin, it provides no teaching whatsoever relating to this protein or its function, much less its role in cellular pathways, including apoptosis. In the absence of any teaching whatsoever of beta catenin, Cowsert fails to teach or suggest a connection between PRKC-iota and beta catenin such that one skilled in the art would recognize that an agent that regulates PRKC-iota expression could be a beta catenin modulating agent. In the absence of any teaching concerning beta catenin and its relationship with PRKC-iota, Cowsert fails to teach or suggest the claimed double assay method of identifying a candidate beta catenin modulating agent. Specifically, Cowsert fails to teach or suggest using a first assay system to detect a change in the expression of PRKC-ι in the presence or absence of a test agent and then using a second assay system to detect a change in the activity of beta catenin in the presence or absence of the test agent.

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Contrary to the Office's assertion, Murray fails to cure the deficiencies of Cowsert. For the reasons set forth above, Murray's measurement of drug-induced apoptosis in K562 cells that over- or under-express PRCK-iota does not render obvious a method of identifying a candidate beta catenin modulating agent using, among other things, an assay system that detects a change in the activity of beta catenin in the presence or absence of a test agent.

Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness because Cowsert and Murray, alone or in combination, fail to teach or suggest all of the limitations of the claimed methods. Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) rejection based on Cowsert and Murray.

Claim 10 was rejected under 35 U.S.C. 103(a) as being unpatentable over Cowsert et al (US 20040014049) and Murray et al (J. Biol. Chem 272(44): 27521-27524, 1997) as applied to claims as 1, 2, 6, 8, and 9 above, and further in view of Summerton et al (Antisense & Nucleic acid Drug Dev. 7: 187-195, 1997) ("Summerton"). Applicants respectfully traverse the rejections.

The Office stated that the teachings of Cowsert and Murray can be combined to render obvious method steps (a)-(g) of claims 1, 2, 6, 8, and 9 by using antisense oligonucleotides as an agent to inhibit PKC iota expression, and that in further combination with the teachings in Summerton, which teaches the use of morpholino phophorodiamidate antisense oligomers, claim 10 is rendered obvious.

Applicants submit that Cowsert and Murray, alone or in combination, fail to teach or suggest a method for identifying a candidate beta catenin modulating agent using a double assay system that involves measuring and detecting a difference in the expression of PRKC- iota in the presence and absence of a test agent and measuring and detecting a change in the activity of beta catenin in the presence and absence of a test agent, for the reasons set forth above. Summerton fails to cure the deficiencies of Murray and Cowsert. Summerton is

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merely a review article directed to morpholino antisense oligomers, which fails to even mention PKC-iota or beta catenin. In the absence of any teaching whatsoever regarding PRKC-iota, much less its use in a double assay system to identify a candidate beta catenin modulating agent, the combined teachings of Murray, Cowsert, and Summerton fail to teach the elements of the claimed invention.

Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness because Murray, Cowsert, and Summerton, alone or in combination, fail to teach or suggest all of the limitations of the claimed methods. Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) rejection based on Murray, Cowsert, and Summerton.

Conclusion

In view of the foregoing amendments and remarks, the applicant submits that the claims are in condition for allowance, which is respectfully solicited. If the examiner believes a teleconference will advance prosecution, he is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

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